



NR3C2 gene

nuclear receptor subfamily 3 group C member 2

Normal Function

The *NR3C2* gene provides instructions for making a protein called the mineralocorticoid receptor. This protein is important in regulating the amount of sodium in the body. Sodium regulation plays a role in blood pressure control and fluid balance. Certain hormones called mineralocorticoids attach (bind) to and turn on (activate) the mineralocorticoid receptor. Aldosterone is one mineralocorticoid that activates the mineralocorticoid receptor. The activated mineralocorticoid receptor acts as a transcription factor, which is a protein that binds to specific regions of DNA and helps control the activity (transcription) of particular genes.

The mineralocorticoid receptor regulates specialized proteins in the cell membrane that control the transport of sodium or potassium into cells. In response to signals that sodium levels in the body are low, the mineralocorticoid receptor increases the number and activity of these proteins at the cell membrane, especially in certain kidney cells. One of these proteins transports sodium into the cell, while another protein simultaneously transports sodium out of the cell and potassium into the cell. These proteins help keep sodium in the body through a process called reabsorption and remove potassium from the body through a process called secretion.

Health Conditions Related to Genetic Changes

pseudohypoaldosteronism type 1

More than 50 mutations in the *NR3C2* gene have been identified in people with pseudohypoaldosteronism type 1 (PHA1), a condition that typically begins in infancy and is characterized by low levels of sodium (hyponatremia) and high levels of potassium (hyperkalemia) in the blood. In particular, *NR3C2* gene mutations are involved in autosomal dominant PHA1, a relatively mild form of the condition that can improve in childhood.

Mutations in the *NR3C2* gene lead to a nonfunctional or abnormally functioning mineralocorticoid receptor protein that cannot properly regulate the specialized proteins that transport sodium and potassium. As a result, sodium reabsorption and potassium secretion are both decreased, causing hyponatremia and hyperkalemia.

other disorders

One particular mutation in the *NR3C2* gene can cause early-onset hypertension with severe exacerbation in pregnancy. People with this condition develop high blood

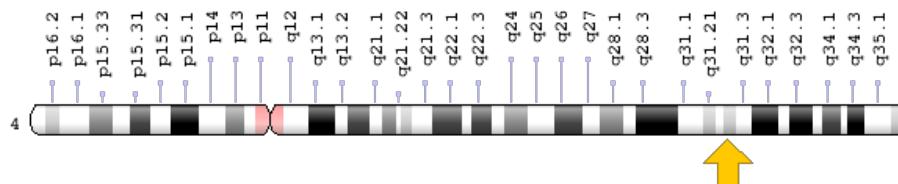
pressure (hypertension) at an early age. The condition can affect males or females, and hypertension worsens in pregnant females.

The mutation involved in this condition changes one protein building block (amino acid) in the mineralocorticoid receptor protein. The amino acid serine is replaced with the amino acid leucine at position 810 in the protein (written as Ser810Leu or S810L). This mutation changes the shape of the receptor, which allows the receptor to be abnormally activated by non-mineralocorticoid hormones such as progesterone and cortisol. The increased mineralocorticoid receptor activity causes excessive sodium reabsorption, which leads to hypertension. Progesterone levels are elevated during pregnancy, which is why the condition worsens in pregnant females.

Chromosomal Location

Cytogenetic Location: 4q31.23, which is the long (q) arm of chromosome 4 at position 31.23

Molecular Location: base pairs 148,078,764 to 148,445,287 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- aldosterone receptor
- FLJ41052
- MCR
- MCR_HUMAN
- MGC133092
- mineralocorticoid receptor
- mineralocorticoid receptor 1
- mineralocorticoid receptor delta
- MLR
- MR

- NR3C2VIT
- nuclear receptor subfamily 3, group C, member 2

Additional Information & Resources

Educational Resources

- Endocrinology: An Integrated Approach (2001): Aldosterone Actions in the Kidney
<https://www.ncbi.nlm.nih.gov/books/NBK26/box/A647/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28NR3C2%5BTIAB%5D%29+OR+%28%28aldosterone+receptor%5BTIAB%5D%29+OR+%28mineralocorticoid+receptor%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

OMIM

- HYPERTENSION, EARLY-ONSET, AUTOSOMAL DOMINANT, WITH SEVERE EXACERBATION IN PREGNANCY
<http://omim.org/entry/605115>
- NUCLEAR RECEPTOR SUBFAMILY 3, GROUP C, MEMBER 2
<http://omim.org/entry/600983>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/NR3C2ID44262ch4q31.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=NR3C2%5Bgene%5D>
- HGNC Gene Family: Nuclear hormone receptors
<http://www.genenames.org/cgi-bin/genefamilies/set/71>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7979
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/4306>
- UniProt
<http://www.uniprot.org/uniprot/P08235>

Sources for This Summary

- Chen SY, Bhargava A, Mastroberardino L, Meijer OC, Wang J, Buse P, Firestone GL, Verrey F, Pearce D. Epithelial sodium channel regulated by aldosterone-induced protein sgk. *Proc Natl Acad Sci U S A*. 1999 Mar 2;96(5):2514-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10051674>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC26816/>
- Geller DS, Farhi A, Pinkerton N, Fradley M, Moritz M, Spitzer A, Meinke G, Tsai FT, Sigler PB, Lifton RP. Activating mineralocorticoid receptor mutation in hypertension exacerbated by pregnancy. *Science*. 2000 Jul 7;289(5476):119-23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10884226>
- Kolla V, Litwack G. Transcriptional regulation of the human Na/K ATPase via the human mineralocorticoid receptor. *Mol Cell Biochem*. 2000 Jan;204(1-2):35-40.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10718622>
- Martinez F, Mansego ML, Escudero JC, Redon J, Chaves FJ. Association of a mineralocorticoid receptor gene polymorphism with hypertension in a Spanish population. *Am J Hypertens*. 2009 Jun; 22(6):649-55. doi: 10.1038/ajh.2009.39. Epub 2009 Mar 26.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19325532>
- OMIM: NUCLEAR RECEPTOR SUBFAMILY 3, GROUP C, MEMBER 2
<http://omim.org/entry/600983>
- Pujo L, Fagart J, Gary F, Papadimitriou DT, Claës A, Jeunemaitre X, Zennaro MC. Mineralocorticoid receptor mutations are the principal cause of renal type 1 pseudohypoaldosteronism. *Hum Mutat*. 2007 Jan;28(1):33-40.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16972228>
- Rafestin-Oblin ME, Souque A, Bocchi B, Pinon G, Fagart J, Vandewalle A. The severe form of hypertension caused by the activating S810L mutation in the mineralocorticoid receptor is cortisone related. *Endocrinology*. 2003 Feb;144(2):528-33.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12538613>
- Riepe FG, Finkeldei J, de Sanctis L, Einaudi S, Testa A, Karges B, Peter M, Viemann M, Grötzinger J, Sippell WG, Fejes-Toth G, Krone N. Elucidating the underlying molecular pathogenesis of NR3C2 mutants causing autosomal dominant pseudohypoaldosteronism type 1. *J Clin Endocrinol Metab*. 2006 Nov;91(11):4552-61. Epub 2006 Sep 5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16954160>
- Viengchareun S, Le Menuet D, Martinerie L, Munier M, Pascual-Le Tallec L, Lombès M. The mineralocorticoid receptor: insights into its molecular and (patho)physiological biology. *Nucl Recept Signal*. 2007 Nov 30;5:e012. doi: 10.1621/nrs.05012. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18174920>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2121322/>
- van Leeuwen N, Caprio M, Blaya C, Fumeron F, Sartorato P, Ronconi V, Giacchetti G, Mantero F, Fernandes-Rosa FL, Simian C, Peyrard S, Zitman FG, Penninx BW, de Kloet ER, Azizi M, Jeunemaitre X, Derijk RH, Zennaro MC. The functional c.-2G>C variant of the mineralocorticoid receptor modulates blood pressure, renin, and aldosterone levels. *Hypertension*. 2010 Nov;56(5):995-1002. doi: 10.1161/HYPERTENSIONAHA.110.155630. Epub 2010 Sep 20.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20855654>

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